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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,052	02/20/2004	Anthony Cerami	CC98-002B04-US	6770

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EXAMINER	
HOLT, ANDRIAE M	
ART UNIT	PAPER NUMBER
1616	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/783,052	CERAMI ET AL.	
	Examiner	Art Unit	
	Andriae M. Holt	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57-76* is/are pending in the application.

4a) Of the above claim(s) *57-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicant's arguments filed November 17, 2008. Claims 57-76 is pending in the application. Claims 57-75 are withdrawn from consideration as being to a non-elected invention. Claim 76 will presently be examined to the extent it reads on the elected subject matter of record.

Rejections not reiterated from the previous Office Action are hereby withdrawn. The following rejections are newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Interpretation

Claim 76 recites means plus function language. Accordingly, the specification is reviewed to determine corresponding structure, material or acts described and equivalents thereof. The specification discloses the perforated container component of the device maintains a diffusion barrier for limiting the passive diffusion of the antigen or an immune cell secretory product or co-stimulatory factor out of a device without limiting the active movement of immune cells into or out of said device (page 14, lines 2-7). The prior art, Watson et al. (GB 2,177,647), disclose a subcutaneously implantable diffusion chamber housing hybrid cells, the chamber has a wall defined by a membrane which, in vivo, inhibits the free diffusion there through of the cells but not subcellular material. Watson et al. disclose the chamber has a main body of generally hollow circular cylindrical form having one end wall, which body is closed at its other end by a filter. Watson et al. further disclose the body is made in two parts, 12 and 13, the former

of which is of similar shape to that of the overall body, while the latter is of sleeve form for threaded engagement about the side wall of part 12 (page 1, lines 59-75). Watson et al. disclose the remaining structure features of the chamber comprise inlet and outlet cannulae 19 and 20 projecting through the end wall of part 12 into and outwardly of the chamber (page 1, lines 76-79). Watson et al. disclose in manufacture, the chamber 10 has been made up from materials and existing products of biologically acceptable forms (page 1, lines 80-90). The chamber disclosed by Watson et al. provides inlet and outlet cannulae that act as perforations to inhibit the free diffusion of hybridoma cells that are housed in the chamber, but not subcellular material. One skilled in the art would recognize the inlet and outlet cannulae disclosed by Watson et al. are interchangeable with the perforations claimed in the instant application. The chamber has a wall defined by a membrane, including the inlet and outlet cannulae, which in vivo, inhibits the free diffusion there through of said cells, but not sub-cellular material.

Thus, the chamber disclosed by Watson et al. would have been considered an equivalent to the "perforated container" that limits the passive diffusion of antigen or immune cell secretory product or co-stimulatory factor, but does not limit the active movement of immune cells into and out of the device at the time the invention was made.

Claim Interpretation

Claim 76 recites or reads on means plus function type language. Accordingly, the specification is reviewed to determine corresponding structure, material or acts

described and equivalents thereof. The specification discloses the perforated container component of the device maintains a diffusion barrier for limiting the passive diffusion of the antigen or an immune cell secretory product or co-stimulatory factor out of a device without limiting the active movement of immune cells into or out of said device (page 14, lines 2-7). The prior art, Piechaczyk et al. (WO 98/27966) teach encapsulated cells producing antibodies, especially antibodies belonging to the various classes of immunoglobulines; IgM, IgD, IgGs, IgE and IgA, and to the use of such encapsulated cells for implantation in vivo for long term delivery or sustained delivery of antibodies of therapeutic interest. Piechaczyk et al. disclose capsules containing cells producing antibodies, which allow the release of the antibodies from the capsules, and which do not elicit inflammatory response after implantation in a host, are provided. Piechaczyk et al. disclose that for optimal function, the capsule pores must meet two criteria. First, they must be large enough to permit molecules of interest, such as antibodies, to exit and to permit the entry and efficient diffusion of nutrients necessary for cell survival. Second, they must be small enough to prevent the encapsulated cells from leaving the capsules and to prevent entry of host immune system cells. The capsule pores disclosed by Piechaczyk et al. act as the perforations to permit entry and efficient diffusion of nutrients necessary for cell survival, but prevent the encapsulated cells from leaving the capsules. One skilled in the art would recognize the capsule pores disclosed by Piechaczyk et al. are interchangeable with the perforations claimed in the instant

application as the pores of the capsules determine the diffusion of material into the capsule, while prohibiting the diffusion of other material outside the capsule.

Thus, the capsule pores disclosed by Piechaczyk et al. would have been considered an equivalent to the "perforated container" that limits the passive diffusion of antigen or immune cell secretory product or co-stimulatory factor, but does not limit the active movement of immune cells into and out of the device at the time the invention was made.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 76 is rejected under 35 U.S.C. 102(b) as being anticipated by Watson et al. (GB 2, 117, 647).

Watson et al. disclose a subcutaneously implantable diffusion chamber housing the hybrid cells, the chamber having a wall defined by a membrane which, in vivo, inhibits the free diffusion there through of the cells but not subcellular material (page 1, lines 25-31). Watson et al. disclose following implantation of the chamber in the patient,

the membrane allows outward diffusion of antibodies out or other active sub-cellular material into the patient, and inward diffusion from the host body of oxygen, nutrients or other subcellular material necessary to sustain the effectiveness of the encapsulated cells. At the same time, the membrane inhibits outward diffusion of the cells themselves and so obviates the risk that these may metastasize as a neoplastic growth or cause other undesirable results in the patient (page 1, lines 32-44). Watson et al. disclose the chamber has a main body of generally hollow circular cylindrical form having one end wall, which body is closed at its other end by a filter. Watson et al. further disclose the body is made in two parts, 12 and 13, the former of which is of similar shape to that of the overall body, while the latter is of sleeve form for threaded engagement about the side wall of part 12 (page 1, lines 59-75). Watson et al. disclose the remaining structure features of the chamber comprise inlet and outlet cannulae 19 and 20 projecting through the end wall of part 12 into and outwardly of the chamber (page 1, lines 76-79) (container with perforations). Watson et al. disclose in manufacture, the chamber 10 has been made up from materials and existing products of biologically acceptable forms (page 1, lines 80-90). Watson et al. disclose hybridoma cells housed in the chamber are denoted generally at 21 in the figure (page 1, lines 91-96). Watson et al. discloses in claim 1 on page 2, a subcutaneously implantable diffusion chamber housing hybrid living cells adapted to produce sub-cellular material capable of affording beneficial activity in the body, the chamber having a wall defined by a membrane, which in vivo, inhibits the free diffusion there through of said cells, but not sub-cellular material.

Watson et al. meet all of the limitations of the claim and thereby anticipate the claim.

Claim 76 is rejected under 35 U.S.C. 102(a) as being anticipated by Piechaczyk et al. (WO 98/27966).

Piechaczyk et al. disclose encapsulated cells producing antibodies, especially antibodies belonging to the various classes of immunoglobulines; IgM, IgD, IgGs, IgE and IgA, and to the use of such encapsulated cells for implantation in vivo for long term delivery or sustained delivery of antibodies of therapeutic interest (page 1, lines 4-8). Piechaczyk et al. disclose capsules containing cells producing antibodies, which allow the release of the antibodies from the capsules, and which do not elicit inflammatory response after implantation in a host (page 6, lines 25-27). Piechaczyk et al. disclose the encapsulated cells according to the invention can be prepared by suspending the cells producing antibodies in an aqueous solution of a polyelectrolyte (e.g. selected from sulphate group-containing polysaccharides or polysaccharide derivatives or of sulphonate group containing synthetic polymers), whereafter the solution in the form of preformed particles is introduced into a precipitation bath containing an aqueous solution of a counter-charged polyelectrolyte (such as for example a polymer with quaternary ammonium groups) (page 6, lines 29-35). Piechaczyk et al. disclose in a preferred embodiment of the invention the cells producing antibodies are encapsulated in a complex consisting of a complex formed from cellulose sulphate and

polydimethyidiallyl-ammonium (page 7, lines 13-15). Piechaczyk et al. disclose the properties of the cellulose capsules, i.e. the size, the pore size, wall thickness and mechanical properties depend upon several factors such as, physical circumstances under which the capsules have been prepared, viscosity of precipitation bath, its ion strength, temperature, rapidity of addition of cell/cellulose sulphate suspension, constitution of cellulose sulphate, as well as other parameters described by the Dautzenberg group (page 7, lines 24-29). Piechaczyk et al. disclose that for optimal function, the capsule pores must meet two criteria. First, they must be large enough to permit molecules of interest, such as antibodies, to exit and to permit the entry and efficient diffusion of nutrients necessary for cell survival. Second, they must be small enough to prevent the encapsulated cells from leaving the capsules and to prevent entry of host immune system cells (page 2, lines 25-29).

Piechaczyk et al. disclose the formulation of capsules on page 7, lines 31-37-page 8, lines 1-16.

Piechaczyk et al. meet all of the limitations of the claim and thereby anticipate the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to

a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 76 is rejected under 35 U.S.C. 103 (a) as being unpatentable over Piechaczyk et al. (WO 98/27966).

Applicant's Invention

Applicant claims a method of immunizing a mammal with an antigen for the preparation of a hybridoma for the production of monoclonal antibody against said antigen, wherein said mammal is immunized by implanting within the body a device. Applicant claims the device is comprised of a porous matrix for containing the antigen within the container having a means for limiting the passive diffusion of the antigen or an immune cell secretory product or co-stimulatory factor out of the device without limiting the active movement of immune cells into or out of said device.

Determination of the scope of the content of the prior art (MPEP 2141.01)

The teachings of Piechaczyk et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Piechaczyk et al. do not teach specifically teach the container limits the passive

diffusion of the antigen or an immune cell secretory product or co-stimulatory factor out of the device without limiting the active movement of immune cells into or out of the device.

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to use the teachings of Piechaczyk et al. and use the capsules taught by Piechaczyk et al. to limit the passive diffusion of the antigen or an immune cell secretory product or co-stimulatory factor out of the device without limiting the movement of immune cells into or out of the device. Piechaczyk et al. teach that for optimal function, the capsule pores must meet two criteria. First, they must be large enough to permit molecules of interest, such as antibodies, to exit and to permit the entry and efficient diffusion of nutrients necessary for cell survival. Second, they must be small enough to prevent the encapsulated cells from leaving the capsules and to prevent entry of host immune system cells. Piechaczyk et al. further disclose properties of the cellulose capsules, i.e. the size, the pore size, wall thickness and mechanical properties depend upon several factors such as physical circumstances under which the capsules have been prepared, viscosity of precipitation bath, its ion strength, temperature, rapidity of addition of cell/cellulose sulphate suspension, constitution of cellulose sulphate, as well as other parameters described by the Dautzenberg group. Therefore, one skilled in the art at the time the invention was made would have been motivated to use the capsule to

limit the passive diffusion of certain materials, without limiting the movement of immune cells because Piechaczyk et al. teach the technology to prepare such capsules. The porous capsules are the container with the perforations (pores) that can be adjusted by the make-up of the capsules to determine which materials are prevented from diffusing out of the capsule, antigens, and which are permitted to diffuse into the capsule, immune cells or nutrients to produce long term delivery or sustained release of antibodies of therapeutic interest.

Therefore, the claimed invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because every element of the invention has been fairly suggested by the cited reference.

None of the claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is (571)272-9328. The examiner can normally be reached on 7:00 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richter Johann can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/John Pak/
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